UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES, AND
TOXIC SUBSTANCES

Note to Reader
August 7, 1998

Background: As part of its effort to involve the public in the implementation of the Food Quality Protection Act of 1996 (FQPA), which is designed to ensure that the United States continues to have the safest and most abundant food supply, EPA is undertaking an effort to open public dockets on the organophosphate pesticides. These dockets will make available to all interested parties documents that were developed as part of the U.S. Environmental Protection Agency's process for making reregistration eligibility decisions and tolerance reassessments consistent with FQPA. The dockets include preliminary health assessments and, where available, ecological risk assessments conducted by EPA, rebuttals or corrections to the risk assessments submitted by chemical registrants, and the Agency's response to the registrants' submissions.

The analyses contained in this docket are preliminary in nature and represent the information available to EPA at the time they were prepared. Additional information may have been submitted to EPA which has not yet been incorporated into these analyses, and registrants or others may be developing relevant information. It's common and appropriate that new information and analyses will be used to revise and refine the evaluations contained in these dockets to make them more comprehensive and realistic. The Agency cautions against premature conclusions based on these preliminary assessments and against any use of information contained in these documents out of their full context. Throughout this process, if unacceptable risks are identified, EPA will act to reduce or eliminate the risks.

There is a 60 day comment period in which the public and all interested parties are invited to submit comments on the information in this docket. Comments should directly relate to this organophosphate and to the information and issues

available in the information in this docket. Once the comment period closes, EPA will review all comments and revise the risk assessments, as necessary.

These preliminary risk assessments represent an early stage in the process by which EPA is evaluating the regulatory requirements applicable to existing pesticides. Through this opportunity for notice and comment, the Agency hopes to advance the openness and scientific soundness underpinning its decisions. This process is designed to assure that America continues to enjoy the safest and most abundant food supply. Through implementation of EPA's tolerance reassessment program under the Food Quality Protection Act, the food supply will become even safer. Leading health experts recommend that all people eat a wide variety of foods, including at least five servings of fruits and vegetables a day.

Note: This sheet is provided to help the reader understand how refined and developed the pesticide file is as of the date prepared, what if any changes have occurred recently, and what new information, if any, is expected to be included in the analysis before decisions are made. **It is not meant to be a summary of all current information regarding the chemical.** Rather, the sheet provides some context to better understand the substantive material in the docket (RED chapters, registrant rebuttals, Agency responses to rebuttals, etc.) for this pesticide.

Further, in some cases, differences may be noted between the RED chapters and the Agency's comprehensive reports on the hazard identification information and safety factors for all organophosphates. In these cases, information in the comprehensive reports is the most current and will, barring the submission of more data that the Agency finds useful, be used in the risk assessments.

Jack Housenger, Acting Director
Special Review and Reregistration
Division

March 12, 1998

MEMORANDUM

SUBJECT: **PHORATE**: Revised HED Chapter of the Reregistration Eligibility Decision Document (RED), Case #0103, PC Code 057201, Barcode D220565

From: Christine L. Olinger, Chemist
Reregistration Branch 1
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Thru: Whang Phang, Ph.D., Branch Senior Scientist
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To: Jason Robertson
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Special Review and Reregistration Division 7508W

The Draft Human Health Assessment for the Reregistration Eligibility Document for phorate is attached which has been revised to include FQPA considerations, the Monte Carlo Dietary Risk Analysis, and the recently submitted reproduction and developmental studies.

It is noted that the acute dietary risk estimated by the Monte Carlo analysis for all population groups exceeds our level of concern at the 99.9 percentile level. The risk is below the level of concern for all population groups at the 95th percentile level.

The label recommendations and labeling rationales concerning the Worker Protection Standard for Sections IV and V of the RED will be addressed later when we are certain they are necessary.

Summary of Confirmatory Data Requirements / Label Changes / Significant Items

1) A neurotoxicity screening battery (acute and subchronic) is required.

2) The requirement for a developmental neurotoxicity study has been reserved, pending the results of the acute and subchronic neurotoxicity studies.

3) HED has recommended for submission of drinking water monitoring studies in order to be able to assess the dietary risk from drinking water resources.

4) Label amendments are required. The restriction against the feeding of sugar beet tops or silage to dairy cattle is considered impractical and should therefore be removed from labels for EPA Reg. Nos. 241-53, 241-145, and 241-257. In addition, a 30-day pregrazing interval has been established for at-cultivation

applications to field corn to control chinch bug nymphs; this pregrazing interval should be extended to the at-cultivation application to field and sweet corn to control corn rootworms (EPA Reg. Nos. 241-53, 241-145, and 241-257).

5) HED concluded that a 12-month plantback restriction was appropriate for root and tuber vegetables, leafy vegetables, and cereal grains. There are currently no rotational crop restrictions on product labels.

6) No tolerances currently exist for field corn stover (fodder), sweet corn stover (fodder), sorghum forage, and wheat hay. Some field residue data have been submitted for these commodities; however, none of the available data reflect the currently registered use patterns for these crops. Therefore, additional field residue data are required for these commodities. In addition, Table 1 (in 860.1000, August 1996) identifies cotton gin byproducts as a raw agricultural commodity of cotton; therefore, field residue data must be submitted for cotton gin byproducts. Tolerances must be proposed for these commodities when adequate field residue data have been submitted.

cc: DMiller (CEB1), BSteinwand (CEB1), YYang (TOX I), MHawkins (for Caswell, microfiche), COlinger (RRB1), JDawson (RRB1), Wphang (RRB1)

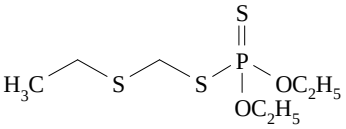
Table of Contents - Phorate HED Chapter

Tables and Figures

A. Physical and Chemical Properties Assessment

DESCRIPTION OF CHEMICAL

Phorate [*O*,*O*-diethyl *S*[(ethylthio)methyl]phosphorodithioate] is a soil and systemic insecticide.



Empirical Formula: $C_7H_{17}O_2PS_3$
Molecular Weight: 260.4
CAS Registry No.: 298-02-2
Shaughnessy No.: 057201

IDENTIFICATION OF ACTIVE INGREDIENT

Technical phorate is a colorless to light yellow clear liquid with a boiling point of 118-120 C. Phorate is slightly soluble in water at 20-50 ppm and soluble in most organic solvents, such as acetone and xylene. It is miscible in alcohols, ethers, ketones, esters, carbon tetrachloride, and vegetable oils. Phorate is subject to hydrolysis under alkaline conditions, but is stable under neutral and acidic conditions.

MANUFACTURING-USE PRODUCTS

A search of the Reference Files System (REFS) conducted 2/17/98 identified three phorate manufacturing-use products (MPs) registered under Shaughnessy No. 057201: the American Cyanamid 85% technical and 85% formulation intermediate (T and FI; EPA Reg. Nos. 241-213 and 241-212, respectively), and the Aceto Agricultural Chemicals Corporation 85% T (EPA Reg. No. 2749-106). We note that although REFS lists label claims of 85% for all three products, the American Cyanamid products are properly identified as 92% formulations (CBRS No. 13228, D199207, 8/24/95, K. Dockter), and Aceto has agreed to modify the label claim to 95% for its technical product (CBRS No. 16229, D219423, 10/6/95, D. Miller). Only the American Cyanamid and Aceto phorate MPs are subject to a reregistration eligibility decision.

The product chemistry data requirements for the American Cyanamid 92% T and 92%

FI (EPA Reg. Nos. 241-213 and 241-212, respectively) and the Aceto Agriculture Chemicals Corporation 95% FI (EPA Reg. No. 2749-106) phorate are all fulfilled. Provided that the registrants either certify that the suppliers of beginning materials and the manufacturing processes for the phorate Ts and FI have not changed since the last comprehensive product chemistry review or submit complete updated product chemistry data packages, HED has no objections to the reregistration of phorate with respect to product chemistry data requirements.

B. Human Risk Assessment

1. Hazard Assessment

a. Acute Toxicity

There are few new acute toxicity studies available for phorate. Essentially all the acute toxicity studies were previously reviewed and published in the Registration Standard for phorate (December, 1988). The acute toxicity data base is adequate for phorate. Table 1 summarizes acute toxicity values and categories for phorate.

Table 1. Acute Toxicity Values for Technical Phorate[1]

Study	Results	Category
Oral LD_{50} - Rat	3.7 mg/kg (M), 1.4 mg/kg (F)	I
Dermal LD_{50} - Rat	9.3 mg/kg (M), 3.9 mg/kg (F)	I
Inhalation LC_{50}- Rat	0.06 mg/L (M), 0.011 mg/L (F)	I
Eye Irritation	Waived[2]	N/A
Dermal Irritation	Waived[2]	N/A
Dermal Sensitization	Waived[2]	N/A

[1] Data are excerpted from the Pesticide Registration Standard for Phorate (Dec. 1988)(p. 8-9).
[2] High acute toxicity prohibits administration of appropriate dose levels.

Technical phorate is highly toxic on an acute oral, dermal, and inhalation basis. The oral LD_{50} values for phorate with rats were 3.7 and 1.4 mg/kg in males and females, respectively (Toxicity Category I). All of the animals that died in this study showed typical clinical signs of cholinergic toxicity such as salivation, lacrimation, exophthalmos, muscle fasciculation and excessive urination and defecation (US EPA, 1988; Newell and Dilley, 1978; MRID# 00126343; satisfies Guideline 81-1).

The dermal LD_{50} values for phorate with rats were 9.3 and 3.9 mg/kg in males and females, respectively (Toxicity Category I). The cholinergic signs noted for the acute oral study were also observed in the acute dermal study (US EPA, 1988; Newell and Dilley, 1978; MRID# 00126343; satisfies Guideline 81-2). In addition, a dermal LD_{50} of 415.6 mg/kg in guinea pigs with typical cholinergic signs noted at higher doses was also reported (Shaffer, 1960; Baron, 1968; MRID# 00139479).

The acute inhalation LC_{50}s for rats were 0.06 and 0.011 mg/L for males and females, respectively (Toxicity Category I), based on a one-hour exposure to analytical grade

phorate aerosol. Typical cholinergic signs were observed in intoxicated animals (US EPA, 1988; Newell and Dilley, 1978; MRID# 00126343; satisfies Guideline 81-3).

There were no acceptable data available on the primary eye or dermal irritation properties of phorate. However, these tests were waived since the high acute toxicity of phorate prohibits the administration of appropriate dosage levels. Likewise, no data are available on the primary dermal sensitization properties of phorate. This study was waived because of the high acute toxicity of phorate (US EPA, 1988).

b. Subchronic Toxicity

There were data available from a 90-day feeding study in rats and a 105-day feeding study in dogs (MRID# 00092873). These studies were conducted in 1956 and were classified as supplementary since the protocols did not adhere to the current guidelines. However, because the toxicity endpoint (cholinesterase inhibition) was satisfactorily identified, and because sufficient data from chronic toxicity studies in rodents and non-rodents were available, additional data from subchronic toxicity studies are not required. Executive summaries of theses two studies follow.

In a 90-day feeding study in rats (Tusing, 1956; MRID# 0092873), phorate was administered in the diet at dosage levels of 0, 0.22, 0.66, 2.0, 6.0, 12.0 or 18.0 ppm (equivalent to 0, 0.011, 0.033, 0.1, 0.3, 0.6, and 0.9 mg/kg/day, respectively) for 90 days. Phorate at 12 and 18 ppm induced mortality as well as reduced body weight gains and food consumption (both sexes). RBC ChE activity was inhibited in females at 2.0 ppm while plasma, RBC and brain ChE activities were inhibited in both sexes at the 6.0 ppm level. The NOEL was 0.66 ppm (0.033 mg/kg/day) and the LOEL was 2 ppm (0.1 mg/kg/day) based on cholinesterase inhibition. The study was classified as supplementary because the histopathology was performed on only 3 (not 10) rats/sex.

In a 105-day feeding study in dogs (Tusing, 1956; MRID# 0092873), technical phorate was administered in capsules to dogs at dosages of 0, 0.01, 0.05, 0.25, 1.25 or 2.5 mg/kg/day, 6 days/week for 13-15 weeks. Each group had 3 dogs (2 males and 1 female) with the exception of the 2.5 mg/kg group, which had 2 males only. The plasma ChE activity was inhibited at a dose of 0.05 mg/kg/day or above (combined sexes). The RBC ChE was inhibited at a dose of 0.25 mg/kg/day or above (combined sexes). All dogs at the 1.25 and 2.5 mg/kg/day levels showed typical cholinergic signs and subsequently died. The NOEL was 0.01 mg/kg/day and the LOEL was 0.05 mg/kg/day based on the reduction of plasma ChE activity. This study was classified as supplementary because only three dogs (2 males and 1 female) per group were used instead of 4 dogs of each sex per group (8 dogs total).

No data are available from 21-day or 90-day dermal toxicity studies with phorate.

These study requirements were waived since the highly toxic nature of phorate prohibits the administration of dosages that could induce adverse effects other than inhibition of cholinesterase activity (US EPA, 1988).

c. Chronic Toxicity and Carcinogenicity

In a combined two-year chronic toxicity/carcinogenicity study in rats (50/sex/group), phorate was administered in the diet (50/sex/group) at dosage levels of 0, 1, 3, or 6 ppm (equivalent to 0, 0.05, 0.15, and 0.3 mg/kg/day, respectively) for 24 months. A NOEL for plasma ChE inhibition in males was not established since the LOEL was 0.05 mg/kg/day, the lowest dose tested (LDT). The NOEL for plasma ChE inhibition in females was 0.05 mg/kg/day while the LOEL was 0.15 mg/kg/day. The NOEL for RBC ChE inhibition was 0.3 mg/kg/day (highest dose tested (HDT)) in males and 0.15 mg/kg/day in females while the LOEL for females was 0.3 mg/kg/day. The NOEL for brain ChE inhibition was 0.15 mg/kg/day in males and 0.05 mg/kg/day in females while the LOELs were 0.3 and 0.15 mg/kg/day for males and females, respectively. The high dose level tested was considered adequate for carcinogenicity testing. Phorate was not considered carcinogenic under the conditions of the study because the treatment did not alter the spontaneous tumor profile in rats (Manus et al., 1981; MRID# 00125233; satisfies Guidelines 83-5, 83-1a, and 83-2a).

In a chronic toxicity study, groups of beagle dogs (6/sex/group) were administered phorate via capsules at doses of 0, 0.005, 0.01, 0.05, or 0.25 mg/kg/day for one year. Compound related effects included slight body tremors in high dose males and females and marginal inhibition of body weight gain in high dose males. The systemic NOEL was 0.05 mg/kg/day and the LOEL was 0.25 mg/kg/day based on body tremors in males and females and inhibited body weight gains in males. The NOEL for plasma ChE inhibition was 0.01 mg/kg/day while the LOEL was 0.05 mg/kg/day for both sexes. The NOEL for RBC or brain ChE inhibition was 0.05 mg/kg/day while the LOEL was 0.25 mg/kg/day for both sexes (Shellenberger and Tegeris, 1987; MRID# 40174527; satisfies Guideline 83-1b).

In a carcinogenicity study, groups of CD-1 mice (50/sex/group) received phorate at a dietary concentration of 0, 1, 3, or 6 ppm (equivalent to 0, 0.15, 0.45, and 0.9 mg/kg/day) for 78 weeks. There were no consistent toxic signs or any non-neoplastic pathologic findings related to test compound administration. The NOEL was 0.45 mg/kg/day and the LOEL was 0.9 mg/kg/day based on a slight decrease in weight gain in females in the first 25 weeks. The dose level tested was considered adequate for carcinogenicity testing based on the results of the range finding study. The treatment did not alter the spontaneous tumor profile in this strain of mice (Manus et al. 1981; MRID# 00124845; satisfies Guideline 83-2(b).

d. Developmental Toxicity

Technical phorate in corn oil was administered by oral intubation to pregnant rats (23 female/group) from day 6 to day 15 of gestation at dosages of 0, 0.125, 0.25, or 0.5 mg/kg/day. No developmental effects were observed in this study at any dosage. The NOEL for both maternal toxicity and developmental toxicity was 0.25 mg/kg/day. The LOEL for each was 0.5 mg/kg/day in which dams exhibited increased mortality, convulsions, and hypothermia while the fetuses showed enlarged hearts. The enlargement of the heart was considered to be a physiologic effect as a result of increased acetylcholine, producing excessive stimulation of the myocardium with ensuing enlargement (Beliles, 1979; MRID# 00122775; satisfies Guideline 83-3a).

Groups of pregnant rabbits (20/group) were administered 0, 0.15, 0.5, 0.9 or 1.2 mg/kg/day of phorate by gavage on days 6-18 of gestation. The maternal NOEL was 0.15 mg/kg/day and the maternal LOEL was 0.5 mg/kg/day based on body weight loss and increased mortality. The developmental NOEL was 1.2 mg/kg/day (the highest dose tested). No developmental effects were observed (Schroeder, 1987; MRID# 40174528; satisfies Guideline 83-3b).

In a developmental toxicity study, pregnant Crl:CD®BR rats (24-25/dose) received oral administration of Phorate (92.1%) in corn oil at dose levels of 0, 0.1, 0.2, 0.3 or 0.4 mg/kg/day from days 6 through 15 of gestation. For maternal toxicity, the NOEL was 0.3 mg/kg/day and the LOEL was 0.4 mg/kg/day, based on increased mortality, clinical signs indicative of neurotoxicity, decreases in body weight and body weight gain and food consumption and gross pathology. Developmental toxicity was manifested as decreased fetal weights and increased incidence of skeletal variations (delayed ossification of the sternum and pelvis). For developmental toxicity, the NOEL was 0.3 mg/kg/day and LOEL was 0.4 mg/kg/day (Lochry, 1990; MRID No. 44422301; satisies Guideline 83-3a).

e Reproductive Toxicity

There was a 3-generation reproductive study in mice (1965; MRID# 00092853) submitted to the Agency. In this study, technical phorate was administered in the diet to mice at dietary levels of 0, 0.6, 1.5 or 3.0 ppm (equivalent to 0, 0.09, 0.23, and 0.45 mg/kg/day, respectively). Compound administration was initiated 7 weeks before the first mating. The study involved 3 generation with 2 litters (a and b) per generation. The only apparent indications of reproductive toxicity were slight reductions in the lactation and viability indices in the F_1b at the highest dose level. The NOEL was estimated to be 1.5 ppm (0.23 mg/kg/day) and the LOEL was 3.0 ppm (0.45 mg/kg/day) based on effects on viability and lactation indices. This 3-generation reproduction study was down-graded from core minimum to unacceptable by the HED/RfD Peer Review Committee (December 30, 1993).

In a two-generation reproduction study, groups of male and female Sprague-Dawley rats (25/sex) were fed diets containing Phorate (92.1%) at dose levels of 0, 1, 2, 4, or 6 ppm (0, 0.087, 0.176, 0.359 or 0.603 mg/kg/day for males and 0, 0.103, 0.210, 0.420 or 0.727 mg/kg/day for females) for two successive generations. For parental systemic toxicity, the NOEL was 0.2 mg/kg/day and the LOEL was 0.4 mg/kg/day based on clinical signs (tremors) and inhibitions of plasma and brain cholinesterase activity (F_1 females only). For offspring toxicity, the NOEL was 0.2 mg/kg/day and the LOEL was 0.4 mg/kg/day based on decreased pup survival and pup body weight. The decrease in pup survival was seen during early lactation and the decrease in pup body weights was seen during the later part of lactation (Schroeder, 1991; MRID No. 44422302; satisfies Guideline 83-4).

f. Mutagenicity

Sufficient data are available to satisfy data requirements for mutagenicity testing. Technical phorate did not induce a genotoxic response in any of the tests listed below.

- Gene mutation assays -

In an Ames assay, phorate was negative at dosages up to 1000 µg/plate with Salmonella typhimurium strains TA100, TA 1535, TA 1537, and TA 1538 in the presence and absence of metabolic activation (Simmon et al., 1977; MRID# 00124901).

A test for reverse mutation in Escherichia coli was negative at dosages up to 1000 µg/plate in the presence and absence of metabolic activation (Simmon et al., 1977; MRID# 00124901).

Phorate did not induce gene mutations at the HGPRT locus in cultured Chinese

hamster ovary (CHO) cells at dosages up to 100 nL/mL with and without metabolic activation (Thilagar et al., 1985; MRID# 00151633).

- Chromosomal aberration assays-

A dominant lethal test in mice was negative at dosages up to 20 mg/kg in the diet (Simmon et al., 1977; MRID# 00124901)

A chromosomal aberrations test was negative in mammalian (rats) bone marrow cells at ip (intraperitoneal) dosages up to 2.5 and 1.5 mg/kg in males and females, respectively (Ivett, 1986; MRID# 00155597).

- Other genotoxic effects studies -

Negative in mitotic recombination assay with Saccharomyces cerevisiae D3 at a concentration of 5% with and without metabolic activation (Simmon et al., 1977; MRID# 00124901).

Preferential toxicity assays in DNA repair-proficient and -deficient strains of Escherichia coli and Bacillus subtillis at a level of 1000 µg/plate were negative (Simmon et al., 1977; MRID# 00124901).

Preferential toxicity assays in DNA repair-proficient and -deficient strains of Bacillus subtilis (strain H17 and M45, respectively) at 1000 µg/plate were negative (Simmon et al., 1977; MRID# 00124901).

Unscheduled DNA synthesis (UDS) assay in human fibroblasts (WI-38 cells) at concentrations up to 10^{-3} M (Mol/L) did not show mutagenic response (Simmon et al., 1977; MRID# 00124901).

g. Metabolism

Data are available from rat metabolism studies in males and females. A single oral dose of 0.8 mg/kg ^{14}C-phorate was administered to male rats. The chemical was readily absorbed and excreted, with approximately 77.2% of the total administered ^{14}C in the urine and 11.7% in the feces within 24 hours. Less than 1% of the total radioactivity was found in tissues (highest level in blood) at 24 hours. Ten metabolites were present in the urine. Two non-phosphorylated metabolites, ethyl (methyl sulfinyl) methyl-sulfone and (ethyl sulfonyl)(methyl-sulfonyl) methane, comprised approximately 71% of the radioactivity present in the urine. About 9% and 10% of the urinary ^{14}C was associated with (O,O-diethyl S-(ethyl sulfonyl) methyl phosphorothioic acid and [(ethyl sulfinyl) methyl, methyl sulfone], respectively. Unchanged parent compound accounted for only 0.5% of the recovered urinary ^{14}C and the remaining four phosphorylated compounds plus one unidentified metabolite together comprised less than 10% of the

urinary radioactivity. These metabolites were formed following cleavage of the sulfur-phosphorus bond associated with the carbon chain in phorate, from methylation of the liberated thiol group, and from oxidation of the resulting sulfide to sulfoxide and sulfone (Hussain, 1987; MRID# 40291601).

Female rats showed a comparable pathway to that described for males (Miller and Wu, 1991; MRID# 41803803).

h. Neurotoxicity

In an acute delayed neurotoxicity study, 14.2 mg/kg (LD_{50} dose) of phorate was administered orally to hens followed by a 21-day interval and a second administration at the same dosage level. Phorate did not cause neurological changes indicative of delayed neurotoxicity (US EPA, 1988; Fletcher, 1984; MRID# 00152640).

No data are available on the acute and subchronic neurotoxicity of phorate. Since phorate is an organophosphate, a neurotoxicity screening battery (acute and subchronic) is required as confirmatory data to support the re-registration of this chemical.

The Agency has received a new developmental toxicity study in rats and a 2-generation reproduction toxicity study in rats that do not show increased susceptibility for infants and children exposed to phorate. In addition, these studies do not demonstrate any findings indicative of effects on the developing nervous system. Although this would provide support for not requiring a developmental neurotoxicity, it was noted that histopathological evaluation of perfused tissue in rats was not available in the data base. Due to concerns regarding the potency of this chemical, and in the absence of this histopathological data, the Hazard Identification Assessment Review Committee (HIARC), at the February 3, 1998 meeting decided to place the requirement for this study under **reserve** status pending receipt of the acute and subchronic neurotoxicity studies.

i. Dermal Absorption

No dermal absorption studies are available. The dermal absorption is considered to be 100% for the purposes of risk assessment because the chemical is very acutely toxic (Tox Category I) by either oral or dermal administration (Toxicology Endpoint Selection Committee meeting of 1/23/96).

j. Other Toxicological Considerations

No data are available on the eye effects of phorate in specialized acute and subchronic

studies. The Toxicology Chapter of the Registration Standard for Phorate (December, 1988) indicated that additional specialized studies are required to determine the potential for phorate to induce adverse ocular effects in acute and subchronic studies in rats and a six month study in dogs, rabbits, or monkeys. The Agency has determined that these studies are no longer required, based on the recommendation of the FIFRA Scientific Advisory Panel (SAP) that these studies should not be routinely required for organophosphate pesticides (March 1997).

Phorate sulfoxide (a phorate metabolite) was administered to rats (35/sex) at dietary levels of 0, 0.32, 0.8 or 2.0 ppm (equivalent to 0, 0.016, 0.04, and 0.10 mg/kg, respectively) for 90 days. Sporadic inhibition of RBC and plasma ChE activity was observed in females at the 0.8 ppm level. At 2.0 ppm, RBC, plasma, and brain ChE activities were inhibited in females while only marginal inhibition of RBC and plasma ChE activity was noted in males. No other dosage-related adverse effects were reported in this study. The NOEL was 0.32 ppm (0.016 mg/kg) and the LOEL was 0.8 ppm (0.04 mg/kg) based on inhibition of plasma and RBC ChE activities (Hutchison at al., 1968; MRID# 00092912).

(Ethylsulfonyl) (methylsulfonyl) methane, a phorate metabolite, has an acute oral LD_{50} value of greater than 5000 mg/kg. In addition, this phorate metabolite does not have the structural properties of a cholinesterase inhibitor. Therefore, this phorate metabolite is not expected to be an acute toxicological concern (Lowe and Fischer, 1987, MRID# 40174526).

Phorate can be metabolized to more potent anticholinesterase compounds through oxidative desulfuration and/or sulfide oxidation. The oxidation products include the sulfoxide and sulfone derivatives of phorate and a phorate oxygen analogue. Findings of the rat metabolism study showed that the oxidized, phosphorylated products represented minor proportions of the phorate metabolites measured in tissues, feces, and urine. Although the phorate sulfoxide metabolite appears to be slightly more toxic than the parent (as demonstrated above in the 90 day rat study with a Phorate) both compounds are very toxic and there is not much difference in their relative toxicity. For this reason, all of the data supporting phorate are adequate to support the metabolites which also inhibit cholinesterase. The Agency reserves the option to require additional toxicity studies with the oxidized metabolites if significant residue levels are detected.

2. Dose Response Assessment

a. Special Sensitivity to Infants and Children

On February 3, 1998 the Hazard Identification Assessment Review Committee met to

evaluate the toxicology database and determine whether sufficient information was available to assess enhanced sensitivity of infants and children exposed to phorate. The developmental toxicity studies showed no increased susceptibility in fetuses as compared to maternal animals following *in utero* exposures in rats and rabbits. Similarly, the two generation reproduction toxicity study in rats showed no increased sensitivity in pups when compared to adults. However, the Committee determined that the **10x** factor to account for enhanced sensitivity of infants and children (as required by FQPA) **should be reduced to 3x** for the following reason: data gap exists for acute and subchronic neurotoxicity studies. Therefore, data on cholinesterase inhibition, neurobehavioral effects (FOB) and histopathology on the central and peripheral nervous system were not available for evaluation after single or repeated exposures to phorate. The Committee also determined that a MOE (Margin of Exposure) of 300 is required for the protection of the general population including infants and children from dietary, occupational and residential exposure to phorate

b. Reference Dose

The HED Hazard Identification Assessment Review Committee established an RfD of 0.0002 mg/kg/day from a one year feeding study in dogs and an uncertainty factor of 300 to account for differences among species, variability among humans, and the neurotoxicity data gaps. The NOEL in the one year feeding study in dogs was 0.05 mg/kg/day and the LOEL was 0.25 mg/kg/day based on body tremors and depression of RBC and brain ChE activity observed in both sexes.

It should be noted that a regulatory value (ADI) of 0.0005 mg/kg/day was established for phorate by the World Health Organization (WHO) in 1994 and verified in 1996. This value is based on a NOEL of 0.05 mg/kg/day from a one-year dog study and an uncertainty factor of 100.

c. Carcinogenicity Classification and Risk Quantification

Phorate has been classified as a group E - "not likely" to be carcinogenic to humans based on carcinogenicity studies in rats and mice in which the treatment did not alter the spontaneous tumor profile in these strains of rats and mice.

d. Developmental Classification

Phorate is not considered a developmental toxicant.

e. Dermal Absorption

No dermal absorption studies are available. The dermal absorption is considered to be 100% for the purposes of risk assessment because the chemical is very acutely toxic

(Tox Category I) by either oral or dermal administration (Toxicology Endpoint Selection Committee meeting of 1/23/96).

f. Other Toxicological Endpoints

A summary of all endpoints may be found in Table 2 on page 14.

i. Acute Dietary

For acute dietary risk assessment, the Health Effects Division Toxicology Endpoint Selection Committee recommended that an endpoint and a dose of 0.05 mg/kg/day from a one-year feeding study in dogs (MRID#40174527) are to be selected based on observations of tremors and inhibition of RBC and brain ChE activities in both sexes of dogs at 0.25 mg/kg/day. A Margin of Exposure of 300 is required to ensure protection from acute dietary exposure to phorate.

This dose was selected for acute dietary risk assessment because the ChE NOEL of this study was comparable to the ChE NOELs observed in 90-day studies with rats and dogs in which ChE activity was measured after six days (rats) or one week (dogs). The 90-day studies were not used to establish any of the toxicological endpoints because these were old studies which did not follow the protocol/current guidelines and were classified as supplementary.

ii. Short, Intermediate and Term Occupational and Residential

The 21-day dermal toxicity study was waived due to the highly corrosive nature of phorate (Tox Category I), which prohibits the administration of doses that could induce adverse effects other than inhibition of ChE activity.

For short and intermediate term occupational and residential risk assessment, the Health Effects Division Toxicology Endpoint Selection Committee recommended that an endpoint and a dose of 0.05 mg/kg/day from a one-year feeding study in dogs (MRID#40174527) are to be selected based on observations of tremors and inhibition of RBC and brain ChE activities in both sexes of dogs at 0.25 mg/kg/day.

iii. Chronic Occupational and Residential (Non-Cancer)

For chronic occupational and non-cancer risk assessment, the Health Effects Division Toxicology Endpoint Selection Committee recommended that an endpoint and a dose of 0.05 mg/kg/day be selected from a one-year feeding study in dogs (MRID#40174527) based on observations of tremors and inhibition of RBC and brain

ChE activities in both sexes of dogs at 0.25 mg/kg/day.

iv. Inhalation (any time period)

Except for an acute inhalation toxicity study, no inhalation toxicity studies are available for selection of a dose and endpoint for a inhalation exposure risk assessment. Based on the LC_{50} value of 0.011 mg/L in females and 0.06 mg/L in males, phorate is placed in Toxicity Category I. Therefore a risk assessment for occupational and residential exposure via this route is required.

An oral NOEL of 0.05 mg/kg/day was selected for inhalation risk assessment because: 1) the lack of appropriate inhalation studies and 2) this dose (NOEL) was also used for acute and chronic dietary as well as dermal exposure risk assesesments.

Since the dose identified for inhalation risk assessment is from an oral study, risk assessments should be as follows:

(i) The inhalation exposure component (mg/L) using a 100 % absorption rate (default value) should be converted to a dosage (mg/kg/day).

(ii) The dermal exposure component (mg/kg/day) should then be added to the above obtained dosage (mg/kg/day).

(ii) This dose should then be compared to the oral NOEL of 0.05 mg/kg/ day to calculate the Margins of Exposure.

Table 2. Summary of Toxicological Endpoints for Phorate

EXPOSURE SCENARIO	DOSE (mg/kg/day)	ENDPOINT	STUDY	MOE REQUIRED
Acute Dietary	NOEL=0.05	Inhibition of RBC and brain cholinesterase activity	Chronic Toxicity - Dog	300
Chronic Dietary	NOEL=0.05	Inhibition of RBC and brain cholinesterase activity	Chronic Toxicity - Dog	300
Short-Term (Dermal) [a]	Oral NOEL=0.05	Inhibition of RBC and brain cholinesterase activity	Chronic Toxicity - Dog	300
Intermediate-Term (Dermal) [a]	Oral NOEL=0.05	Inhibition of RBC and brain cholinesterase activity	Chronic Toxicity - Dog	300
Long-Term (Dermal) [a]	Oral NOEL=0.05	Inhibition of RBC and brain cholinesterase activity	Chronic Toxicity - Dog	300
Inhalation (Any time period) [a]	Oral NOEL=0.05	Inhibition of RBC and brain cholinesterase activity	Chronic Toxicity - Dog	300

a = Appropriate route-to-route extrapolations should be performed for these risk assessments [i.e., the dermal and inhalation exposure components using the appropriate absorption rates (100% default value for dermal and for inhalation) should be converted to equivalent oral doses and compared to the oral NOEL).

3. Dietary Exposure and Risk Characterization

a. Dietary Exposure (Food Sources)

i. 860.1200 Directions for Use

A REFS search conducted 2/17/98 identified three phorate end-use products (EPs) registered to American Cyanamid Company. These EPs as well as all active SLN registrations are listed in Table 3 below.

Table 3. Phorate end-use products (EPs) with food/feed uses registered to American Cyanamid Company and all active SLN registrations.

EPA Reg. No. SLN No.	Acceptance Date	Formulation	Product Name
241-53	6/94	10% G	Thimet® 10-G Soil and Systemic Insecticide
241-145	4/97	15% G	Thimet® 15-G Soil and Systemic Insecticide
241-257 [a]	8/96	20% G	Thimet® 20-G Soil and Systemic Insecticide
LA920014, MT910004, OR890005, WA870010, WA910013, WI910004	--	20% G	Clean Crop Phorate 20 G
ME910001, NC910006, OR920025, WA910007	--	12% G	Tenax™ [b]
OR880002, WA930001	--	10% G	Rampart 10-G Soil and Systemic Insecticide
WA920005, WI910006	--	20% G	Phorate 20-G

[a] Including SLN No. LA920011.
[b] This product is an EUP (34704-EUP-11).

Label amendments are required. The restriction against the feeding of treated sugar beet tops or silage to dairy cattle is considered impractical (refer to 860.1000) and should therefore be removed from labels for EPA Reg. Nos. 241-53, 241-145, and 241-257. In addition, a 30-day pregrazing interval has been established for at-cultivation applications to field corn to control chinch bug nymphs; this pregrazing interval should be extended to the at-cultivation application to field and sweet corn to control corn rootworms (EPA Reg. Nos. 241-53, 241-145, and 241-257).

In addition, a 12 month plant back restriction is appropriate for root and tuber vegetables, leafy vegetables, and cereal grains.

ii. 860.1300 Nature of the Residue - Plants

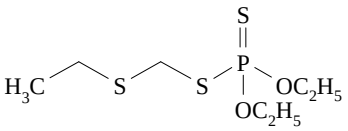
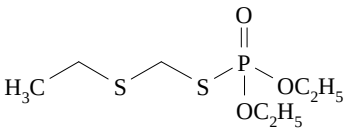
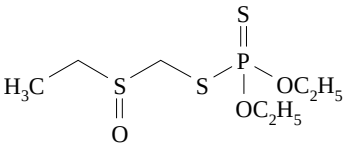
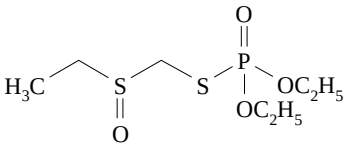
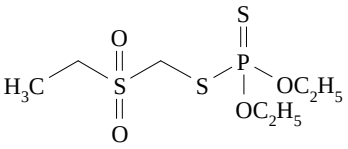
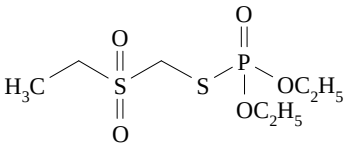
The qualitative nature of the residue in plants is adequately understood based on studies with alfalfa, beans, carrots, corn, cotton, lemons, oats, and peas. The residues of concern in plant commodities are phorate, phorate sulfoxide, phorate sulfone, phorate oxygen analog, phorate oxygen analog sulfoxide, and phorate oxygen analog sulfone. The metabolism data indicate that phorate is metabolized in plants by oxidation of the thioether sulfur and then the thiono sulfur to yield the sulfoxides and sulfones of phorate and phorate oxygen analog. Some hydrolysis of the sulfoxides and sulfones may also occur. The chemical names and structures of the residues of concern are depicted in Figure A.

The current tolerance expression is for the combined residues of phorate and its cholinesterase-inhibiting metabolites. For Codex harmonization, the tolerance expression should be revised to read as follows: the tolerances listed in 40 CFR §180.206 are established for the combined residues of the insecticide phorate (O,O-diethyl S[(ethylthio) methyl]phosphorodithioate), phorate sulfoxide, phorate sulfone, phorate oxygen analog, phorate oxygen analog sulfoxide, and phorate oxygen analog sulfone.

iii. 860.1300 Nature of the Residue - Livestock

The qualitative nature of the residue in animals is adequately understood based on the results of acceptable ruminant and poultry metabolism studies. The residues of concern in animal commodities are phorate, its oxygen analog, and their corresponding sulfoxides and sulfones. The metabolism study in *ruminants* indicates that phorate is metabolized by cleavage of the sulfur-phosphorus bond resulting in a thiolate compound which may then undergo methylation. Oxidation of the sulfur in the methylated metabolite results in various non-phosphorylated metabolites which may be further metabolized and/or incorporated into natural products. In a *poultry* metabolism study, no residues of phorate, its oxygen analog, or their sulfoxides and sulfones were detected in *poultry* tissues or eggs.

Figure A. Chemical Structures of Phorate Residues of Concern

 **Phorate**: O,O-diethyl S-[(ethylthio)methyl] phosphorodithioate	 **Phorate oxygen analog**: O,O-diethyl S-[(ethylthio)methyl] phosphorothioate
 **Phorate sulfoxide**: O,O-diethyl S-[(ethylsulfinyl)methyl] phosphorodithioate	 **Phorate oxygen analog sulfoxide**: O,O-diethyl S-[(ethylsulfinyl)methyl] phosphorothioate
 **Phorate sulfone**: O,O-diethyl S-[(ethylsulfonyl)methyl] phosphorodithioate	 **Phorate oxygen analog sulfone**: O,O-diethyl S-[(ethylsulfonyl)methyl] phosphorothioate

iv. 860.1340 Residue Analytical Methods - Plants and Animals

The Pesticide Analytical Manual (PAM) Volume II lists ten methods (Method I and nine "lettered" methods) for the enforcement of tolerances for phorate residues of concern in/on plant and animal commodities. Most listed methods (using GC, IR-spectroscopy, or TLC techniques) determine combined residues of phorate, phorate sulfoxide, phorate sulfone, phorate oxygen analog, phorate oxygen analog sulfoxide, and phorate oxygen analog sulfone by oxidation to phorate oxygen analog sulfone. The stated limits of detection range from 0.008 to 0.01 ppm.

Residue analytical methods for livestock commodities are no longer required because CBRS has recommended for revocation of animal analytical methods.

v. 860.1360 Multiresidue Methods

The FDA PESTDATA database dated 1/94 (PAM Volume I, Appendix I) indicates that phorate, phorate sulfoxide, phorate sulfone, phorate oxygen analog, phorate oxygen

analog sulfoxide, and phorate oxygen analog sulfone are completely recovered (>80%) using Multiresidue method Section 302 (Luke method; Protocol D). Phorate sulfoxide, phorate oxygen analog, phorate oxygen analog sulfoxide, and phorate oxygen analog sulfone are not recovered using Sections 303 (Mills, Onley, Gaither method; Protocol E, nonfatty) and 304 (Mills fatty food method; Protocol E, fatty). Recovery of phorate was variable and recovery of phorate sulfone was <50% using Sections 303 and 304.

vi. 860.1380 Storage Stability

Adequate storage stability data are available to support any established or reassessed tolerances in plant and animal commodities. Storage stability studies have been submitted demonstrating that residues of phorate, phorate sulfoxide, and phorate sulfone are stable for at least 2 years of frozen storage in/on dry beans, potatoes, and sugar beet roots and tops, and for at least 1.5 years in/on corn grain, forage, and fodder, and wheat grain, forage, and straw. Weathered residues of phorate were stable in corn meal and oil stored frozen for 1 year. Residues of phorate oxygen analog, phorate oxygen analog sulfoxide, and phorate oxygen analog sulfone were found to be stable for at least 2 years of frozen storage in/on dry beans. HED concludes from this information that the requirement for submission of storage stability data for phorate and its regulated sulfoxide and sulfone metabolites to support the crop field trial data is satisfied.

Storage stability data are available for milk. Phorate-related residues are stable in milk for a period of at least 4 days when stored under refrigeration and are stable for a period of at least two months when stored frozen. Since milk samples from the ruminant feeding study were stored for no longer than ca. 4-6 weeks, HED concludes that there are no storage stability concerns associated with milk. Although no storage stability studies were performed on other ruminant tissues, these samples were stored for only 4-6 weeks and HED will not require that storage stability studies be performed with these commodities.

vii. 860.1500 Crop Field Trials

The reregistration requirements for magnitude of the residue in/on coffee; field corn forage; field corn grain; sweet corn (K+CWHR); sweet corn forage; hops; peanuts; potatoes; sorghum fodder; sorghum grain; soybeans; sugar beet roots; sugar beet tops; sugarcane; wheat forage; wheat grain; and wheat straw have been satisfied. The available data indicate that the tolerance levels can be reduced for the following commodities: beans (succulent and dry); field corn grain, sweet corn (K+CWHR), potatoes, sorghum grain, soybeans, and sugarcane. The requirements for aspirated grain fractions data for field corn, sorghum, soybeans, and wheat were waived based on nondetectable residues found in/on grain/seed from field residue studies reflecting

exaggerated rates.

No tolerances currently exist for field corn stover (fodder), sweet corn stover (fodder), sorghum forage, and wheat hay. Some field residue data have been submitted for these commodities; however, none of the available data reflect the currently registered use patterns for these crops. Therefore, additional field residue data are required for these commodities. In addition, Table 1 (in 860.1000 of the Residue Chemistry Guidelines, August 1996) identifies cotton gin byproducts as a raw agricultural commodity of cotton; therefore, field residue data must be submitted for cotton gin byproducts. Tolerances must be proposed for these commodities when adequate field residue data have been submitted. It is not expected that these data will significantly change the risk assessment; therefore, the data are considered confirmatory.

Food and feed additive tolerances have been proposed by IR-4 for dried and spent hops, respectively, at 2 ppm; HED previously recommended for these tolerance proposals pending submission of adequate supporting storage stability data and method validation data. Because all storage stability concerns have been resolved for phorate residues of concern, no additional data are required to support this tolerance petition. However, the petitioner should be advised that a tolerance is no longer required for spent hops and that dried hops are now considered to be a RAC; the tolerance level of 2 ppm is appropriate for dried hops.

The established tolerances for bean vines and peanut vines should be revoked since the Agency no longer considers these commodities to be significant livestock feed items (Table 1, 860.1000, August 1996). In addition, the established tolerance for peanut hay should be revoked since a restriction against the feeding of this commodity exists.

No registered uses of phorate currently exist for the following crops for which tolerances have been established: alfalfa, barley, Bermuda grass, lettuce, rice, and tomatoes. Therefore the established tolerances for these crops should be revoked.

The existing tolerances and the reassessment of these tolerances are summarized in Table 4.

viii. 860.1520 Processed Food/Feed

The reregistration requirements for magnitude of the residue in the processed commodities of coffee, cottonseed, peanuts, potatoes, sorghum, soybeans, sugar beets, sugarcane, and wheat are fulfilled.

The requirements for processing studies with cottonseed, field corn, sorghum,

soybeans, and wheat were waived based on nondetectable residues found in/on grain/seed from field residue studies reflecting exaggerated rates.

The available sugar beet processing data indicate that phorate residues of concern do not concentrate in dried sugar beet pulp. Therefore, the established feed additive tolerance for this commodity should be revoked.

The existing tolerances and the reassessment of these tolerances are summarized in Table 4.

ix. 860.1480 Meat, Milk, Poultry, and Eggs

There are no registered direct animal treatments for phorate on cattle, goats, hogs, horses, sheep, or poultry. The requirements for a poultry feeding study were waived based on the results of the metabolism study. Although HED previously determined that the established tolerances for poultry commodities should remain in effect, HED now believes that given the reassessed tolerances and changes in Table 1 (860.1000 August 1996), poultry commodities can be considered to be a 180.6(a)(3) situation and current poultry and egg tolerances can be revoked.

The registrant performed a ruminant feeding study in which animals were dosed at 1.39 and 3.1 ppm; the latter value is considered to represent the maximum practical dietary burden given that greater doses resulted in clinical symptoms of organophosphate poisoning and death. Since detectable residues were not found in any ruminant tissues or milk when dosed at this maximum level, HED has concluded that a 180.6(a)(3) situation exists with respect to ruminant commodities and the current tolerances should be revoked.

x. 860.1400 Water, Fish and Irrigated Crops

Phorate is presently not registered for direct use on potable water and aquatic food and feed crops; therefore, no residue chemistry data are required under these guideline topics.

xi. 860.1460 Food-Handling Establishments

Phorate is presently not registered for use in food-handling establishments; therefore, no residue chemistry data are required under this guideline topic.

xii. 860.1850 Confined Accumulation in Rotational Crops

An adequate confined rotational crop study, reflecting plantback intervals (PBIs) of 9 and 12 months, has been submitted. Based on the results of the study, HED concluded that a 12-month plantback restriction was appropriate for root and tuber vegetables, leafy vegetables, and cereal grains but that the submitted data did not support a crop rotation restriction for peas. Additional data are required for peas.

xiii. 860.1900 Field Accumulation in Rotational Crops

Limited field rotational crop studies with peas must be submitted in order to obtain a plant-back interval. HED noted that if shorter plantback intervals were desired for root and tuber vegetables, leafy vegetables, and cereal grains, then limited field rotational crop studies would be required. There are currently no rotational crop restrictions on product labels.

The registrant subsequently submitted a confined rotational crop study reflecting a 4-month PBI to replace the 9- and 12-month PBI study. HED concluded that this study is unacceptable because the fallow land was regularly irrigated prior to planting of the rotational crops. HED required that the registrant either propose a 12 month plant back interval or submit limited field rotational crop studies at the desired plant-back interval.

xiv. Tolerance Reassessment Table

The tolerances listed in 40 CFR §180.206 are expressed in terms of phorate and its cholinesterase-inhibiting metabolites. To harmonize with the expression for Codex MRLs for residues of phorate, the tolerance expression should be revised as follows: the tolerances listed in 40 CFR §180.206 are for the combined residues of the insecticide phorate (*O*,*O*-diethyl *S*[(ethylthio) methyl]phosphorodithioate), phorate sulfoxide, phorate sulfone, phorate oxygen analog, phorate oxygen analog sulfoxide, and phorate oxygen analog sulfone.

<u>Tolerances Listed Under 40 CFR §180.206:</u>

Sufficient field trial data reflecting the maximum registered use patterns are available to ascertain the adequacy of the established tolerances for: coffee, beans, green; corn, field, forage; corn, sweet, forage; cottonseed; hops, cones, dried; peanuts; sorghum, fodder; sugar beet, roots; sugar beet, tops; wheat, forage; wheat, grain; and wheat, straw. The available data indicate that the tolerance levels can be reduced for the following commodities: beans (succulent and dry); field corn grain; sweet corn (K+CWHR); potatoes; sorghum grain; soybeans; and sugarcane.

The established tolerances for milk, eggs, and the fat, meat, and meat byproducts of cattle, goats, hogs, horses, sheep, and poultry can be revoked. HED has determined that this represents a 180.6(a)(3) situation and tolerances are not required.

The tolerance level for hops must be increased to reflect that fact that the RAC is now considered to be dried hops and not fresh hops. Adequate data are available to support a dried hops tolerance.

Because the Agency no longer considers bean vines and peanut vines to be significant livestock feed items, the established tolerances for these commodities should be revoked. The established tolerance for peanut hay should also be revoked since a restriction against the feeding of treated peanut hay exists on current product labels.

No registered uses of phorate currently exist on the following crops for which tolerances have been established: alfalfa, barley, Bermuda grass, lettuce, rice, and tomatoes. The established tolerances for the commodities of these crops should be revoked.

Sufficient data are available to assess the adequacy of the established tolerances for dried sugar beet pulp. These data indicate that phorate residues of concern do not concentrate in dried sugar beet pulp; therefore, the established feed additive tolerance should be revoked.

Tolerances To Be Proposed:

When adequate field trial data have been submitted, the registrant must propose a tolerance for field and sweet corn stover (fodder), cotton gin byproducts, sorghum forage, and wheat hay.

A summary of phorate tolerance reassessments is presented in Table 4.

Table 4. Tolerance Reassessment Summary for Phorate.

Commodity	Current Tolerance (ppm)	Tolerance Reassessment (ppm)	Comment/ *[Correct Commodity Definition]*
Tolerances Listed Under 40 CFR §180.206:			
Alfalfa (fresh)	0.5	Revoke	No registered uses.
Alfalfa hay	1	Revoke	No registered uses.
Barley grain	0.1	Revoke	No registered uses.
Barley straw	0.1	Revoke	No registered uses.
Bean vines	0.5	Revoke	Not considered a significant feed item (Table 1, 860.1000).
Beans	0.1	0.05	Residues from the registered uses do not exceed the 0.05 ppm level *[Beans, succulent and dry]*
Bermuda grass straw	0.5	Revoke	No registered uses.
Cattle, fat	0.05	Revoke	180.6(a)(3)
Cattle, meat	0.05		
Cattle, meat byproducts	0.05		
Coffee beans	0.02	0.02	*[Coffee, beans, green]*
Corn grain	0.1	0.05	Residues from registered uses do not exceed 0.05 ppm for Codex harmonization. *[Corn, field, grain]*
Corn forage	0.5	0.5	*[Corn, field, forage]* *[Corn, sweet, forage]*
Cottonseed	0.05	0.05	*[Cotton, undelinted seed]*
Eggs	0.05	Revoke	180.6(a)(3)
Goats, fat	0.05	Revoke	180.6(a)(3)
Goats, meat	0.05		
Goats, meat byproducts	0.05		
Hogs, fat	0.05	Revoke	180.6(a)(3)
Hogs, meat	0.05		
Hogs, meat byproducts	0.05		
Hops	0.5	2.0	*[Hops, cones, dried]*

(*continued; footnotes follow*)

Table 4. Tolerance Reassessment Summary for Phorate.

Commodity	Current Tolerance (ppm)	Tolerance Reassessment (ppm)	Comment/ *[Correct Commodity Definition]*
Horses, fat	0.05	Revoke	180.6(a)(3)
Horses, meat	0.05		
Horses, meat byproducts	0.05		
Lettuce	0.1	Revoke	No registered uses.
Milk	0.02	Revoke	180.6(a)(3)
Peanut vines	0.3	Revoke	Not considered a significant feed item (Table 1, 860.1000).
Peanut hay	0.3	Revoke	Feeding restriction exists.
Peanuts	0.1	0.1	
Potatoes	0.5	0.2	Residues from the registered uses do not exceed 0.2 ppm for Codex harmonization.
Poultry, fat	0.05	Revoke	180.6(a)(3)
Poultry, meat	0.05		
Poultry, meat byproducts	0.05		
Rice	0.1	Revoke	No registered uses.
Sheep, fat	0.05	Revoke	180.6(a)(3)
Sheep, meat	0.05		
Sheep, meat byproducts	0.05		
Sorghum fodder	0.1	0.1	*[Sorghum, fodder]*
Sorghum grain	0.1	0.05	Residues from the registered uses do not exceed 0.05 ppm for Codex harmonization. *[Sorghum, grain]*
Soybeans	0.1	0.05	Residues from registered uses do not exceed 0.05 ppm for Codex harmonization.
Sugar beet roots	0.3	0.3	*[Sugar beets, roots]*
Sugar beet tops	3	3	*[Sugar beets, tops]*
Sugarcane	0.1	0.05	Residues from the registered uses do not exceed 0.05 ppm.
Sweet corn (K+CWHR)	0.1	0.05	Residues from the registered uses do not exceed 0.05 ppm. *[Corn, sweet (K+CWHR)]*
Tomatoes	0.1	Revoke	No registered uses.

(*continued; footnotes follow*)

Table 4. Tolerance Reassessment Summary for Phorate.

Commodity	Current Tolerance (ppm)	Tolerance Reassessment (ppm)	Comment/ *[Correct Commodity Definition]*
Wheat grain	0.05	0.05	*[Wheat, grain]*
Wheat (green fodder)	1.5	1.5	*[Wheat, forage]*
Wheat straw	0.05	0.05	*[Wheat, straw]*
Tolerances Listed Under 40 CFR §186.4750:			
Dried sugarbeet pulp	1	Revoke	Available data indicate that residues do not concentrate.
Tolerances to be Proposed:			
Corn, field, stover (fodder)	--	TBD[1]	
Corn, sweet, stover (fodder)	--	TBD	
Cotton, gin byproducts	--	TBD	
Sorghum, forage	--	TBD	
Wheat, hay	--	TBD	

1. TBD = To be determined. Residue data are outstanding.

xiv. Codex Harmonization

The Codex Alimentarius Commission has established several maximum residue limits (MRLs) for phorate residues in various commodities (see *Guide to Codex Maximum Limits For Pesticide Residues, Part 2, FAO CX/PR, 4/91*). The Codex and U.S. tolerance expressions will be in harmony when the U.S. tolerance expression is revised to specify phorate, phorate sulfoxide, phorate sulfone, phorate oxygen analog, phorate oxygen analog sulfoxide, and phorate oxygen analog sulfone. A comparison of the Codex MRLs and the corresponding **reassessed** U.S. tolerances is presented in Table 5.

The following conclusions can be made regarding efforts to harmonize the U.S. tolerances with the Codex MRLs with respect to MRL/tolerance level: (I) compatibility between the U.S. tolerances and Codex MRLs exists for beans, cottonseed, eggs, field corn grain (maize), potatoes, sorghum, soybeans, and wheat; and (ii) incompatibility of the U.S. tolerances and Codex MRLs remains for field corn forage, peanuts, and sugar beet roots and tops because of differences in agricultural practices; no questions of compatibility exist with respect to commodities where Codex MRLs have been established but U.S. tolerances do not exist or will be revoked.

Table 5. Codex MRLs and applicable U.S. tolerances. Recommendations for compatibility are based on conclusions following reassessment of U.S. tolerances (see Table 4).

Codex			Reassessed U.S. Tolerance (ppm)	Recommendation And Comments
Commodity (As Defined)	MRL [1] (mg/kg)	Step		
Barley	0.05	CXL	Revoke	No registered uses in U.S.
Carrot	0.2 [2]	7B	--	No registered uses in U.S.
Common bean (pods and/or immature seeds)	0.1	CXL	0.1	Compatibility exists.
Cotton seed	0.05	CXL	0.05	Compatibility exists.
Eggs	0.05 *	CXL	Revoke	
Beet fodder	0.05	CXL	--	No registered uses in U.S.
Maize	0.05	6	0.05	Compatibility exists.
Maize fodder	0.2	8	TBD [3]	
Maize forage	0.1	5	0.5	
Meat	0.05 *	CXL	Revoke	
Milk	0.05 *	8	Revoke	
Peanut	0.05	7B	0.1	
Peanut oil, crude	0.05 *	5	--	
Peanut oil, edible	0.05 *	5	--	
Potato	0.2	7B	0.2	Compatibility exists.
Rape seed	0.1	CXL	--	No registered uses in U.S.
Sorghum	0.05	CXL	0.05	Compatibility exists.
Soya bean (dry)	0.05	CXL	0.05	Compatibility exists.
Sugar beet	0.05	8	0.3	
Sugar beet leaves or tops	1	8	3	
Tomato	0.1	CXL	Revoke	No registered uses in U.S.
Wheat	0.05	CXL	0.05	Compatibility exists.

1. An asterisk (*) signifies that the MRL was established at or about the limit of detection.
2. Decreased from 0.5 ppm by 1993 JMPR.
3. TBD = To be determined. Residue data are outstanding.

b. Dietary Exposure (Drinking Water Source)

A drinking water health advisory level for phorate and/or the phorate metabolites has not been established. Hydrolysis and microbial degradation appear to be the most

important means of phorate dissipation in the environment. Phorate is very unstable to photolysis in water, but photolysis in the field may not be important since phorate degrades rapidly by hydrolysis and aerobic soil metabolism. Also, phorate is incorporated or knifed in to a depth where sunlight does not contribute to its degradation. Phorate rapidly photolyses in water to form formaldehyde and phorate sulfoxide.

Parent phorate degrades in water with half-lives of 3 days at pH's 5, 7, and 9. Parent phorate is very mobile to essentially immobile in soil (Freundlich K_{ads} values of 1.5-20) depending on the soil organic carbon content, but is not persistent in aerobic soil ($T_{1/2}$=3 days). In soil, parent phorate degrades into the oxidized metabolites phorate sulfoxide and sulfone. These metabolites are more persistent ($T_{1/2}$'s of 65 and 137 days, respectively) than parent phorate and more mobile, based on a laboratory soil column leaching study and a terrestrial field dissipation study that demonstrated significant mobility in soil. These metabolites are more likely to be present in water resources than parent phorate because they are more persistent and mobile.

i. Ground Water

EFED has provided estimated environmental concentrations (EECs) for residues of phorate in ground water using the SCI-GROW model. Values were calculated for corn, beans, cotton, peanuts, potatoes, sorghum, soybeans, sugar beets, sugar cane, and wheat, and ranged from 0.004 μ/L for corn to 0.015 μg/L for peanuts.

EPA's "Pesticides in Ground Water Database" reports no detections in 3,341 samples that have been submitted to date for parent phorate. This is consistent with the results of the laboratory and field dissipation studies, in which no downward mobility in soil of parent phorate was observed. Also, the metabolites phorate sulfoxide and sulfone were not detected in 12 samples, as reported in the Pesticides in Ground Water Database. However, the 12 samples reported do not represent a statistically significant body of data. The environmental fate data indicate that the metabolites would likely be detected in shallow ground water underlying permeable soils if more extensive sampling were conducted. Phorate sulfoxide and sulfone were detected to 12-18 inches of depth in a terrestrial field dissipation study in Georgia with permeable soils and normal rainfall.

ii. Surface Water

EFED has provided estimated environmental concentrations (EEC), which are upper bound estimates of parent phorate concentrations in surface water, using PRZM/EXAMS 2.3 modeling. This value is likely an over-estimate of what would be expected in drinking water, since the model is based on a single 10 hectare field with a 1 hectare pond, and does not represent an entire watershed and any dilution which may occur. The EECs were estimated for corn, beans, cotton, peanuts, potatoes,

sorghum, soybeans, sugar beets, sugar cane, and wheat. The highest values were obtained for the cotton scenario: 22.8 μg/L for acute risk (1 in 10 year maximum) and 0.1 μg/L for chronic risk (1 in 10 year average).

Monitoring studies have been conducted for phorate only in the Mississippi Basin, Illinois, Colorado, and Florida. Analyses from an IL study were reported as total phorate + sulfoxide + sulfone. No monitoring data are available for the metabolites. Only two detects were noted for the Colorado agricultural watershed (out of 25) at concentrations ranging from 0.08 μg/L to 0.6 μg/L. Phorate was not detected in any of the other samples from any of the other studies. The monitoring data are likely to be of little utility for dietary risk assessment, since the oxidized metabolites are more likely to be present than the parent, but in almost all of the studies, analyses for the metabolites were not conducted.

c. Dietary Risk Assessment and Characterization

i. Chronic Dietary Risk from Food Sources

A chronic dietary analysis was conducted using a Reference Dose (RfD) of 0.0002 mg/kg body weight/day (refer to section 2.b. for discussion of endpoint). The chronic dietary analysis was also based on: 1) all of the published tolerances and foods listed in the Tolerance Index System (TIS) and 40 CFR §180.206 or the reassessed tolerance levels (see Table 4), whichever value is greater; and 2) assumed 100% of the crops were treated to estimate the theoretical maximum residue contribution (TMRC) for the general population and 22 subgroups. This analysis is considered a high-end estimate or *"worst-case estimate"* of the dietary exposure.

The results of the chronic dietary analysis indicate the TMRCs for the U.S. population in general and many of the population subgroups greatly exceeded 100% of the RfD; therefore, an additional analysis was conducted using percent crop treated values and CBRS recommendations for tolerance reassessments. Results of these analyses for selected population sub-groups are presented in Table 6.

Table 6. Summary of Phorate Chronic Dietary Risk Analysis (Food Source)

Population Group	Percent RfD using TMRC[1]	Percent RfD using AR[2]
U.S. Population	761	35
Non-nursing Infants	421	11
Children 1-6	1640	71
Children 7-12	1182	53

[1]TMRC = Total Maximum Residue Contribution. Does not incorporate anticipated residues or reassessed

tolerances.
[2]ARs = Anticipated Residues. Risk analysis includes use of percent crop treated provided by BEAD (12/97) and CBRS recommendations for reassessed tolerances (including revocation of meat and milk tolerances).

Drinking water was not included in this dietary risk analysis. When the **recommendations** for reassessed tolerances are considered in the risk analysis, including revocation of all meat and milk tolerances, then the chronic dietary risk from food sources only, is below our level of concern. It is noted that the Food Quality Protection Act requires re-evaluation of percent crop treated values every five years whenever they are used in a dietary risk assessment.

ii. Acute Dietary Risk from Food Sources

An acute dietary toxicological endpoint of concern has been identified based on cholinesterase inhibition (refer to section 2f.i. for a discussion of the acute dietary endpoint).

The detailed acute dietary exposure analysis evaluates individual food consumption as reported by respondents in the USDA 1977-78 Nationwide Food Consumption Survey (NFCS) and estimates the distribution of single day exposures through the diet for the U.S. population and certain subgroups. The analysis assumes uniform distribution of phorate in the commodity supply. Since the toxicological effect to which high end exposure is being compared is cholinesterase inhibition in this analysis, all standard DRES subgroups are of concern. The analysis includes the U.S. population-48 states and four subgroups: Infants (<1 year), children (1-6 years), females (13+ years) and males (13+ years).

The margin of exposure (MOE) is a measure of how closely the high end exposure comes to the NOEL (the highest dose at which no effects were observed in the laboratory test), and is calculated as the ratio of the NOEL to the exposure (NOEL/exposure = MOE). When the NOEL is derived from an animal study and the Agency has concerns about the enhanced sensitivity of infants and children, the Agency is not generally concerned unless the MOE is below 300 for phorate only.

Two acute dietary analyses were conducted for phorate by the Agency. The first acute dietary analysis was conducted using all existing published tolerances. This is considered an absolute worst-case scenario of the acute dietary risk. The second/refined acute dietary analysis was conducted with anticipated residues (as appropriate) and the phorate uses being supported under reregistration (see Table 4). Anticipated residues were provided as follows:

-No processed sugar commodity residues were used in the analysis since residues are destroyed by the lime and carbonation process.
-According to cooking studies, residues in baked, boiled and fried potatoes are

reduced by 3.5x, 9.3x, and 2.6x, respectively. The anticipated residues for baked, boiled and fried potatoes used in the analysis are 0.057 ppm, 0.022 ppm and 0.077 ppm, respectively.
-No concentration factor was used for dried potato granules since according to processing studies, no concentrating occurs.
-For corn, soybeans, and wheat, all of the field trials indicated non-detectable residues (<0.05 ppm) so an anticipated residue of 0.025 ppm (half the limit of detection) was used for this analysis.

The results of the acute dietary analysis are summarized in Table 7.

Table 7. Summary of Phorate Acute Dietary Risk Analysis (Food Source)

Population	Acute MOE[1,2]	Refined Acute MOE[1,3]
General population	6	13
Infants <1	4	8
children 1-6	4	8
females 13+	8	25
males 13+	8	13

[1] These high-end percentile MOEs generally indicate a risk concern if less than 300
[2] based on published tolerances (see table 4)
[3] based on reassessed tolerances (see table 4) and anticipated residues as indicated above in the text.

Both the acute and refined acute dietary analyses resulted in MOEs considerably less than 300 which generally indicate a possible risk concern. The acute analysis assumes maximum/tolerance level residues on all of the commodities (that have tolerances) and that all of these commodities were treated with phorate. This represents the worst-case scenario. The refined acute analysis used anticipated residues for blended commodities to reflect residues that more closely approximate those levels consumed by the population.

The registrant has submitted an acute dietary risk analysis conducted by Novigen using DEEM software, which uses Monte Carlo simulations to estimate the Margins of Exposure to multiple sub-populations. The analysis used food consumption data from the 1989-1992 USDA CSFII survey, information on the percent of crop treated (from a 1996 BEAD memo), and data from field trial studies. A summary of the estimated MOEs at the 99th percentiles and above are presented in table 8.

Table 8. Novigen-Calculated Exposures and MOEs for Food Only at 99th-, 99.5th-, and 99.9th Percentiles of Exposure

Subgroup	Percentile	Exposure (mg/kg/day)	MOE
General U.S. Population	99	0.00013	384
	99.5	0.000192	260
	99.9	0.000405	124
Children (1-6)	99	0.000307	163
	99.5	0.000401	125
	99.9	0.00078	64
Children (7-12)	99	0.000196	255
	99.5	0.000262	191
	99.9	0.000489	102
Infants	99	0.000084	598
	99.5	0.000149	336
	99.9	0.000441	113
Females 13 +	99	0.000091	547
	99.5	0.000128	390
	99.9	0.000257	195

HED has reviewed this analysis (D. Miller, 1/29/98) and has noted several deficiencies with the assumptions used when conducting the analysis. However correction of each deficiency would probably only minimally affect the risk so it is unlikely that recalculating the MOEs would reduce the risk sufficiently below the level of concern. The risk exceeds our level of concern at the 99.9 percentile for all population sub-groups. It is still exceeded at the 99th percentile for children 1-6 and 7-12. The risk becomes acceptable between the 99 and 97.5 percentiles for children 7-12 and between 97.5 and 95 for children 1-6.

iii. Drinking Water Risk (Acute and Chronic)

Ground Water SCI-GROW is a model for estimating concentrations of pesticides in ground water under "worst-case" conditions. The estimates derived for phorate are consistent with the monitoring data, and are likely to be somewhat representative of the metabolite concentrations as well. The SCI-GROW and monitoring values for concentration of phorate in water are considerably below the levels at which there is a acute or chronic dietary risk concern. Therefore the Agency has no concern about dietary risk from exposure to phorate in ground water.

Surface Water As described in Section B.3.b.ii. previously in this document, the monitoring data are insufficient for accurately assessing the exposure to phorate from surface water. The risk estimated using EECs calculated for surface water

using the PRZM/EXAMS model exceeds the level of concern for drinking water. In fact, the levels of concern for both acute and chronic dietary risk are exceeded for water alone, without even taking food sources into consideration. This model was not designed to estimate the levels in drinking water from a particular watershed, but can be used as a screening tool to identify pesticides which may have potential dietary risk concerns. For example, the PRZM model simulates a farm pond, and does not account for dilution, water treatment, movement (rivers, creeks), or turnover (reservoirs). HED recommends that the registrant conduct monitoring studies to provide the Agency with better information on the levels of phorate and its metabolites in drinking water from surface water sources.

4. Occupational and Residential Exposure and Risk Characterization

a. Occupational and Residential Exposure

An occupational exposure assessment has been conducted since toxicological criteria are triggered and there is a potential exposure to handlers (mixers, loaders, applicators, etc.) during use or to persons entering treated sites after application is complete.

i. Summary of Use Patterns and Formulations: Occupational and Residential

Phorate is an organophosphate insecticide and nematicide formulated as a granular (6.5 to 20 percent ai) and as an emulsifiable concentrate manufacturing product (92 to 95 percent ai). There are no current registrations for greenhouse or indoor uses of phorate, but currently there are two 24(c) registration for application at-planting to field-grown lilies.

Phorate can be applied by aircraft and ground equipment (soil band treatment, soil in-furrow treatment, soil drill treatment, soil side dress treatment). The maximum application rates range from 1.3 to 3.9 lb ai/acre. Only one application per season is allowed for most of the uses. Two applications per season are allowed for irrigated cotton, sorghum, peanuts and sugar beets. The interval between applications ranges from 1 to 2 months.

At this time products containing phorate are intended primarily for occupational uses and <u>not</u> for homeowner uses; therefore, no residential exposures are expected.

ii. Mixer/Loader/Applicator Exposure Assessment and Exposure Tables

EPA has determined that there are potential exposures to loaders, applicators, or other handlers for usual use-patterns associated with phorate. Based on the use patterns and potential exposures described above, four major exposure scenarios were identified for phorate:

(1a) loading the granular formulation for aerial application;
(1b) loading the granular formulation for ground applications;
(2) applying the granular formulation with aerial equipment;
(3) applying the granular with ground equipment; and
(4) flagging for the aerial application of the granular formulation.

The minimum and maximum application rates (1.0 and 3.9 lb ai/A, respectively) were used in this assessment to represent the range of all crops, including the lily use. <u>For example</u>, aerial applications for corn represents the minimum application rate for all labeled aerial sites. The MOE resulting from the minimum application was so low, a maximum aerial application site was not presented (see Tables 8, 9, and 10)

It should be noted that aerial applications to soybeans, peanuts, or potatoes would result in exposure to loaders and applicators

that would exceed that for aerial corn applications, since the rates per acre for those crops are double to triple that for corn.

Short-term and intermediate-term exposure assessments are presented in Table 9.

iii. Post- Application Exposure Assessment

Soil dissipation studies for potatoes and peanuts indicated low soil residues present suggesting possible post application exposures. The need for post application exposure studies will be determined pending the outcome of handler post application risk mitigation decisions.

Table 9. Short-Term and Intermediate-Term Occupational Exposure to Phorate

Exposure Scenario (Scen. #)	Baseline Dermal Unit Exposure[a] (mg/lb ai)	Baseline Inhalation Unit Exposure[b] (μg/lb ai)	Representative Crop and Application Rate[c] (lb ai/acre)	Daily Acres Treated[d]	Daily Dermal Exposure[e] (mg/day)	Daily Inhalation Exposure[f] (mg/day)	Daily Total Exposure[g] (mg/day)
Loader Exposure							
Granular Formulation for Aerial Application (1a)	0.0048	1.7	Corn[h] = 1.0	500	2.4	0.9	3.3
Granular Formulation for 6 & 8 Row Planters (1b)	0.0048	1.7	Typical Acres Treated at Maximum Rates				
			Sugarcane[h] = 4.0	69	1.32	0.47	1.8
				100	1.92	0.68	2.60
			Wheat[h] = 1.0	69	0.33	0.12	0.45
				100	0.48	0.17	0.65
			Maximum Acres Treated at Maximum Rates				
			Sugarcane[h] = 4.0	213	4.1	1.4	5.5
			Wheat[h] = 1.0	213	1.0	0.36	1.4
Applicator Exposure							
Aerial - Fixed-Wing - enclosed cockpit (2)	No data - see engineering controls	No data - see engineering controls	Corn[h] = 1.0	500	No data - see engineering controls	No data - see engineering controls	No data - see engineering controls
Granular Formulation for 6 & 8 Row Planters (3)	No data - see engineering controls	No data - see engineering controls	Typical Acres Treated at Maximum Rates				
			Sugarcane[h] = 4.0	69	No data - see engineering controls	No data - see engineering controls	No data - see engineering controls
				100	No data - see engineering controls	No data - see engineering controls	No data - see engineering controls
			Wheat[h] = 1.0	69	No data - see engineering controls	No data - see engineering controls	No data - see engineering controls
				100	No data - see engineering controls	No data - see engineering controls	No data - see engineering controls
			Maximum Acres Treated as Maximum Rate				
			Sugarcane[h] =4.0	213	No data - see engineering controls	No data - see engineering controls	No data - see engineering controls
			Wheat[h] = 1.0	213	No data - see engineering controls	No data - see engineering controls	No data - see engineering controls
Flagger Exposure							
Granular Applications (4)	0.00025	0.15	Corn[h] = 1.0	500	1.3	0.08	1.33

[a] Baseline dermal unit exposures represent long pants, long sleeve shirts, no gloves, open loading, enclosed cockpit for aerial application, open cab tractor.

(Continued, footnotes follow)

b Baseline inhalation unit exposure does not include the use of a respirator.
c Application rate from phorate labels (EPA Reg. Nos. 34704-259 and 9779-293, 34704-712).
d Acres treated are based on the Corn Insecticide Cluster Risk Assessment, Nov/1993.
e Daily Dermal Exposure (mg/day) = Dermal Unit Exposure (mg/lb ai) * Max. Appl. Rate (lb ai/acre) * Max. Treated (acres).
f Daily Inhalation Exposure (mg/day) = Inhalation Unit Exposure (mg/lb ai) * Max. Appl. Rate (lb ai/acre) * Max. treated
g Daily Total Exposure (mg/day) = Daily Dermal Exposure (mg/day) + Daily Inhalation Exposure (mg/day).
h The crops selected in this table REPRESENT the minimum and/or maximum application rates for the use sites for this chemical. These exposure and risk determinations are considered to be all inclusive and not crop specific.

b. Occupational and Residential Risk Assessment/Characterization

i. Risk from Dermal and Inhalation Exposures Equations and Tables

The daily dose is calculated using the following formula:

$$Daily\ Dose\left(\frac{mg}{Kg\ Day}\right) = Daily\ Exposure\left(\frac{mg}{Day}\right) \cdot \left(\frac{1}{Body\ Weight\ (Kg)}\right) \cdot (Percent\ Absorption)$$

The short term and intermediate term margin of exposure (MOE) estimating risk was calculated using the following formula:

$$MOE = \frac{NOEL\left(\frac{mg}{kg\ day}\right)}{Daily\ Dose\left(\frac{mg}{kg\ day}\right)}$$

Table 10 presents the risk assessments for short-term and intermediate-term occupational exposures, while Table 11 summarizes the assumptions and parameters specific to each exposure scenario and corresponding risk assessment. No chronic exposure scenarios were identified. The exposure assessments are based on PHED V1.1 data.

Table 10: Short-Term and Intermediate-Term Occupational Risk from Phorate

Exposure Scenario (Number)	Repre-sentative Crop	Baseline Total Dose (mg/kg/day)[a]	Baseline Dermal MOE[b]	Risk Mitigation Measures							
				Additional PPE[c]				Engineering Controls[d]			
				Dermal Unit Exposure (mg/lb ai)	Inhalation Unit Exposure (μg/lb ai)	Daily Total Dose (mg/kg/day)[a]	Total MOE[b]	Dermal Unit Exposure (mg/lb ai)	Inhalation Unit Exposure (μg/lb ai)	Daily Total Dose (mg/kg/day)[a]	Total MOE[b]
Loader Risk											
Granular Formulation for Aerial Application (1a)	Corn	0.047	1	0.0016	0.43	0.01	5	0.0001	0.034	0.001	50
Granular Formulation for 6 and 8 Row Planters (1b)	Typical Acres Treated at Maximum Rates[e]										
	Sugarcane	0.03	2	0.0016	0.43	0.0078	6	0.0001	0.034	0.00041	120
		0.04	1	0.0016	0.43	0.011	5	0.0001	0.034	0.00077	65
	Wheat	0.006	8	0.0016	0.43	0.002	25	0.0001	0.034	0.0001	500
		0.009	5	0.0016	0.43	0.003	17	0.0001	0.034	0.0002	250
	Maximum Acres Treated at Maximum Rates[f]										
	Sugarcane	0.08	0.63	0.0016	0.43	0.024	2	0.0001	0.034	0.0016	31
	Wheat	0.02	3	0.0016	0.43	0.006	8	0.0001	0.034	0.0004	130
Applicator Risk											
Aerial- Fixed-wing - enclosed cockpit (2)	Corn	No data see engineering controls	No data see engineering controls	No data see engineer-ing controls	No data see engineer-ing controls	No data see engineering controls	No data see engineer-ing controls	0.0017	1.32	0.023	2
Granular Formulation with 6 and 8 Row Planters (3)	Typical Acres Treated at Maximum Rates[e]										
	Sugarcane	No data see engineering controls	No data see engineering controls	No data see engineer-ing controls	No data see engineer-ing controls	No data see engineering controls	No data see engineer-ing controls	0.0022	0.22	0.0095	5
										0.014	4

(Continued, footnotes follow)

Table 10: Short-Term and Intermediate-Term Occupational Risk from Phorate

Exposure Scenario (Number)	Repre-sentative Crop	Baseline Total Dose (mg/kg/day)[a]	Baseline Dermal MOE[b]	Risk Mitigation Measures							
				Additional PPE[c]				Engineering Controls[d]			
				Dermal Unit Exposure (mg/lb ai)	Inhalation Unit Exposure (μg/lb ai)	Daily Total Dose (mg/kg/day)[a]	Total MOE[b]	Dermal Unit Exposure (mg/lb ai)	Inhalation Unit Exposure (μg/lb ai)	Daily Total Dose (mg/kg/day)[a]	Total MOE[b]
	Wheat	No data see engineering controls	No data see engineering controls	No data see engineer-ing controls	No data see engineer-ing controls	No data see engineering controls	No data see engineer-ing controls	0.0022	0.22	0.0024	21
										0.0035	14

(Continued, footnotes follow)

Table 10: Short-Term and Intermediate-Term Occupational Risk from Phorate

Exposure Scenario (Number)	Repre-sentative Crop	Baseline Total Dose (mg/kg/day)[a]	Baseline Dermal MOE[b]	Risk Mitigation Measures							
				Additional PPE[c]				Engineering Controls[d]			
				Dermal Unit Exposure (mg/lb ai)	Inhalation Unit Exposure (μg/lb ai)	Daily Total Dose (mg/kg/day)[a]	Total MOE[b]	Dermal Unit Exposure (mg/lb ai)	Inhalation Unit Exposure (μg/lb ai)	Daily Total Dose (mg/kg/day)[a]	Total MOE[b]
Granular Formulation with 6 & 8 Row Planters (3)	Maximum Acres Treated at Maximum Rates[f]										
	Sugarcane	No data see engineering controls	No data see engineering controls	No data see engineer-ing controls	No data see engineer-ing controls	No data see engineering controls	No data see engineer-ing controls	0.0022	0.22	0.029	2
	Wheat	No data see engineering controls	No data see engineering controls	No data see engineer-ing controls	No data see engineer-ing controls	No data see engineering controls	No data see engineer-ing controls	0.0022	0.22	0.0074	7
Flagger Risk											
Granular Applications (4)	Corn	0.019	3	0.0013	0.038	0.009	6	0.00005	0.003	0.00038	130

a Daily Total dose (mg/kg/day) = (daily dermal exposure (mg/day) + daily inhalation exposure (mg/day)) / 70 kg.
The daily dose is calculated using the following formula: daily dose (mg/kg/day) = daily exposure (mg/day) / body weight (kg)
b MOE = NOEL (0.05 mg/kg/day)/daily dermal dose (mg/kg/day).
c Additional PPE is represented by double layer of clothing, chemical resistant gloves and dust/mist respirator.
d Engineering Controls is represented by closed system (i.e., lock'n load and enclosed cabs and cockpits); single layer clothing and no gloves.
e 69 acres/day and 100 acres/day, respectively - refer to Table 9.
f 213 acres/day - refer to Table 9.

Table 11. Exposure Scenario Descriptions for Uses of Phorate

Exposure Scenario (Number) Data source PHED V1.1	Standard Assumptions (8-hr work day)	Comments
Loader Exposure		
Loading Granulars (1a and 1b)	For aerial application - 500 acres. For 6 and 8 row planters 69, 100, and 213 acres	**Baseline:** "Best Available" grades: Dermal and inhalation acceptable grades, hand exposure all grades. Dermal = 29 to 36 replicates; inhalation = 58 replicates; hand = 10 replicates. Low confidence in dermal data, high confidence in inhalation data. **PPE:** Dermal, inhalation and hand acceptable grades. Dermal = 29 to 36 replicates; inhalation = 58 replicates; hand = 45 replicates. Medium confidence in dermal data, high confidence in inhalation data. PHED data used for baseline, no protection factors (PFs) were necessary. For additional PPE, a 50% PF was used for the addition of coveralls. For engineering controls, a 98% PF was applied to the baseline for closed mixing.
Applicator Exposure		
Aerial-Fixed Wing -- enclosed cockpit -- Granular (2)	500 acres.	**Baseline/Engineering Controls:** "Best Available" grades: Dermal exposure grade C data; inhalation and hand exposure all grades. Dermal = 9 to 13 replicates; inhalation = 13 replicates; hand = 4 replicates. Low confidence in dermal and inhalation data. PHED data used for baseline/engineering, no PFs were necessary.
Granular 6 and 8 Row Planters (3)	69, 100, and 213 acres.	**Engineering Control:** "Best Available" grades: Dermal, inhalation and hand exposure acceptable grades. Dermal = 27 to 30 replicates; inhalation = 37 replicates; hands = 24 replicates. High confidence in dermal and inhalation data. PHED data used for engineering controls, no PFs were necessary.
Flagger		
Flagging - Granulars (4)	500 acres.	**Baseline:** "Best Available" grades: Dermal, inhalation and hand exposure all grades. Dermal = 16 to 20 replicates; inhalation = 4 replicates; and, hand = 4 replicates. Low confidence in dermal and inhalation data. PHED data used for baseline, or 50% PF was applied to total deposition.

ii. Incident Reports

In addition to use of margins of exposure to estimate the risk, incident data are considered. The following data bases were consulted for poisoning incident data on the active ingredient phorate:

- OPP Incident Data System (IDS);
- Poison Control Centers - (data received in response to 1993 Data-Call-In covering the years 1985 to 1992);
- California Department of Food and Agriculture (Replaced by Department of Pesticide Regulation 1991); and,
- National Pesticide Telecommunication Network (NPTN).

IDS (as of 12/95) received 18 separate incident reports, most involving wildlife and ecological adverse effects. Poison Control Centers Data (1985 to 1992) showed 109 cases of occupational and 82 cases of non-occupational exposure to phorate. California data (1982-1993) showed 22 cases of adverse reactions to phorate. NPTN (1985-1991) handled 116 calls on phorate involving 39 incidents (29 humans, 5 animals, and 5 other, e.g. plants, wildlife).

As a result of a Data Call-In (DCI) by the Agency in 1993, OPP received poisoning control center data from 1985-1992 for 28 organophosphates and carbamate chemicals. The percent of occupational exposures to phorate alone or in combination with other chemicals which resulted in both symptoms and life-threatening symptoms exceeded the median score for the 28 chemicals analyzed. Phorate was ranked in the top 25% of (these 28) chemicals most frequently associated with adverse effects that had symptomatic or life-threatening outcomes.
Non-occupational exposure to phorate, whether alone or in combination with other chemicals, exceeded the median score for the number of cases referred to a health care facility (HCF). (The Poison Control Centers classified workers indirectly exposed, i.e., non-handlers, as non-occupational exposures.) Of the 28 chemicals, phorate ranked 6 for occupational exposure and 7 for non-occupational exposure, with number 1 being most frequently associated with adverse effects. This suggests that phorate is above average in its ability to cause adverse effects. Therefore, regulatory restrictions to prevent acute poisoning should be in accordance with other organophosphates that are above average. When using the California data and calculating ratios for the number of systemic poisonings per 1,000 applications, the calculations for phorate are higher than the median score for the 28 chemicals. Note, however, that California calculations were based on a relatively small number of cases. When using U.S. data, the ratios for exposure per use, poisonings per use, health care referral per use and hospital admitted cases per use were below the median scores. However, it should be considered that these 28 chemicals were selected for a Data-Call-In because of

concerns about the incidence of poisonings in California agricultural workers. Approximately one-third of children exposed to phorate, whether alone or in combination with other chemicals, were referred to a HCF.

The following conclusions can be drawn from the detailed California Incident Data from 1982-1993.

1. Symptoms of a systemic illness are more likely reported after phorate exposure as compared to ocular and dermal effects.

2. Applicators and mixer/loaders are the most frequently affected activity categories.

3. Phorate is currently only used in granular formulations. Some of the above average ratios or measures of hazard (described above) suggest that handlers may not fully observe precautions because of the perception that poisoning is much less likely with a granular than liquid formulation. Label requirements for these products need to be as stringent as for liquids. A prominent label warning that failure to follow precautions may be expected to result in serious or even life-threatening poisoning requiring immediate medical care should be considered. Also, the following may be added, "This granular formulation is soluble and is readily absorbed across skin to cause poisoning."

iii. Occupational Risk Characterization

The MOEs for each occupational exposure scenario are summarized in Table 12. Even though a chronic toxicological endpoint for risk assessment has been identified a chronic risk assessment is not necessary because chronic occupational exposures are not expected based on the existing use patterns.

Table 12. Summary of the Short Term and Intermediate Term Occupational Margins of Exposure (MOEs)[1]

Exposure Scenario	MOE	MOE with EPA risk mitigation techniques
Granular Formulation for Aerial Application / *Loaders*	1	50
Granular formulation for 6 and 8 Row Planters / *Loaders*	1 - 5	31, 65, 130-500
Aerial fixed-wing enclosed cockpit / *Applicators*	-[2]	2
Granular formulation with 6 and 8 Row Planters / *Applicators*	--	2 - 14
Granular Application / *Flaggers*	3	130

[1] The exposure and risk described in Tables 9 through 12 are all inclusive and **NOT crop specific** determinations.
[2] no data available.

MOEs of less than 300 generally trigger a risk concern. The calculations of risk indicate that the MOEs are less than 300 despite maximum mitigation measures (engineering controls) for short-term risk and intermediate-term risk for all but two of the exposure scenarios. The MOEs are equal to or greater than 300 with engineering controls for short-term risk and intermediate-term risk for following scenarios:

- Loading the granular formulation into ground application equipment; and
- Flagging for aerial application of granular formulation for corn only.

These two scenarios having the lowest occupational risk are based on marginal exposure data. The scenario "granular formulation with 6 and 8 row planters for applicators" having MOEs of 2 - 14 is the only exposure scenario based on high confidence exposure data. The toxicological endpoint (cholinesterase inhibition) was observed in several animal studies in addition to the critical study on which the MOEs are based. The risk assessment for the one scenario "granular formulation with 6 and 8 row planters for applicators" is a fairly realistic risk assessment. The remaining scenarios may be an underestimation of risk if the MOEs were to correlate more closely with the MOEs of the high confidence exposure data. The excessive risk described by

the MOEs appears to correspond with the incident data described above.

Although a chronic (noncancer) toxicological endpoint has been identified for phorate, a chronic exposure for workers is not expected based on the current use patterns. For this reason, a chronic risk assessment is not applicable.

c. Statement of the Adequacy of the Residential Exposure Database to Assess Infant's and Children's Exposures

Phorate is only applied to agricultural crops or to field-grown nursery stock. Accordingly, the Agency has no residential exposure concerns for infants and children, and no data are required to assess such exposure.

5. Aggregate Exposure and Risk Assessment/Characterization

The Agency has no concerns for the general U.S. population, including infants and children, from residential exposure to phorate. Therefore only dietary exposures to phorate need be consider in the aggregate assessments.

a. Acute Aggregate Exposure and Risk

The Agency does not have sufficient reliable data to quantitate the risk from water, but the information which is available suggests that there is a potential acute dietary risk concern from water. The total dietary exposure from water and food sources cannot be combined for a total dietary or aggregate risk. The MOEs calculated to assess the acute dietary risk for food range from 8 to 13, which is well below 300, the level which the Agency considers acceptable. However, since there are risk concerns individually for food and water, the aggregate risk would certainly be unacceptable.

b. Chronic Aggregate Exposure and Risk

The Agency does not have sufficient reliable data to quantitate the risk from water, but the information which is available suggests that there is a potential chronic dietary risk concern from water. The total dietary exposure from water and food sources cannot be combined for a total dietary or aggregate risk. Using refined exposure values for foods, the chronic risk is estimated to be 155% to 314% of the RfD, which is greater than 100%, the level which the Agency considers acceptable. However, since there are risk concerns individually for food and water, the aggregate risk would certainly be unacceptable.

6. Other Food Quality Protection Act Considerations

a. Cumulative Risk

Section 408(b)(2)(D)(v) of the Food Quality Protection Act requires that, when considering whether to establish, modify, or revoke a tolerance, the Agency consider "available information" concerning the cumulative effects of a particular pesticide's residues and "other substances that have a common mechanism of toxicity." The Agency believes that "available information" in this context might include not only toxicity, chemistry, and exposure data, but also scientific policies and methodologies for understanding common mechanisms of toxicity and conducting cumulative risk assessments. For most pesticides, although the Agency has some information in its files that may turn out to be helpful in eventually determining whether a pesticide shares a common mechanism of toxicity with any other substances, EPA does not at this time have the methodologies to resolve the complex scientific issues concerning common mechanism of toxicity in a meaningful way. EPA has begun a pilot process to study this issue further through the examination of particular classes of pesticides. The Agency hopes that the results of this pilot process will increase the Agency's scientific understanding of this question such that EPA will be able to develop and apply scientific principles for better determining which chemicals have a common mechanism of toxicity and evaluating the cumulative effects of such chemicals. The Agency anticipates, however, that even as its understanding of the science of common mechanisms increases, decisions on specific classes of chemicals will be heavily dependent on chemical specific data, much of which may not be presently available.

Although at present the Agency does not know how to apply the information in its files concerning common mechanism issues to most risk assessments, there are pesticides as to which the common mechanism issues can be resolved. These pesticides include pesticides that are toxicologically dissimilar to existing chemical substances (in which case the Agency can conclude that it is unlikely that a pesticide shares a common mechanism of activity with other substances) and pesticides that produce a common toxic metabolite (in which case common mechanism of activity will be assumed).

EPA does not have, at this time, available data to determine whether phorate has a common mechanism of toxicity with other substances or how to include this pesticide in a cumulative risk assessment. For the purposes of this tolerance action, therefore, EPA has not assumed that phorate has a common mechanism of toxicity with other substances.

b. Endocrine Disruption

The Agency is required to develop a screening program to determine whether certain substances (including all pesticides and inerts) "may have an effect in humans that is

similar to an effect produced by a naturally occurring estrogen, or such other endocrine effect..." The Agency is currently working with interested stakeholders, including other government agencies, public interest groups, industry and research scientists in developing a screening and testing program and a priority setting scheme to implement this program. Congress has allowed 3 years from the passage of FQPA (August 3, 1996) to implement this program. At that time, EPA may require even further testing of phorate for endocrine disruptor effects.

c. Determination of Safety (U.S. Population, Infants, and Children)

Using the most reliable data available to the Agency at this time, the levels of concern from dietary exposure to phorate from food and water each are exceeded. Therefore, HED cannot recommend for the reregistration of this pesticide as we cannot make a determination that there is a reasonable certainty of no harm from the use of phorate.